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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,725	05/12/2005	Hidenori Abe	10525.0006	7083

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EXAMINER	
JARRELL, NOBLE E	

ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
11/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,725	ABE ET AL.	
	Examiner	Art Unit	
	Noble Jarrell	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20,22,24,26 and 27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *5-7,12 and 13* is/are allowed.

6)☒ Claim(s) *1-4,8-11,13-20,22,24,26 and 27* is/are rejected.

7)☒ Claim(s) *1 and 27* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/21/2005;9/1/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of group I in the reply filed on 11/01/07 is acknowledged. The traversal is on the ground(s) that the requirements for restriction were not properly demonstrated. This is not found persuasive because formula I can be classified differently depending upon what cyclic group is present for variable Z or Za, for example. If the ring is piperidine, the class/subclass is 546/184. If the ring is azepane, the class/subclass is 540/484.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 2, 14-20, 22, 24, and 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the salts of the parent compound of formula I, does not reasonably provide enablement for the prodrugs of the parent compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants adequately show the preparation of the elected group and species, and their salts. However, applicants are not enabled for prodrugs of these compounds. Banker (*Modern Pharmaceutics,* **1996**, 597*)* teaches that the identification of a prodrug requires finding the

correct chemical modification. Once that is determined, extensive testing for the safety and efficacy of the prodrug (considered a different entity) is required.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth herein below:

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to tryptophan derivatives that contain a benzene ring.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

Banker shows that prodrugs require the identification of the correct chemical modification. In addition, once a prodrug is developed, it is considered a new entity and requires safety and efficacy testing.

(5) The relative skill of those in the art:

One of ordinary skil in the art is a chemist familiar with the synthetic techniques used in the specification.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for preparation of the elected group and species.

However, the specification does not provide guidance for the preparation of prodrugs of the elected group and species.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to claims 2, 14-20, 22, 24, and 26, and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

Claim Objections

4. Claims 1 and 27 are objected to because of the following informalities: these claims contain non-elected subject material. Appropriate correction is required.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-4, 8-10. 14, and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Alburn et al. (US 3,268,515, issued August 23, 1966). Alburn et al. report compounds 10 and 11 of column 3, which both anticipate the elected group. In these compounds, variable R^1 or R^2 is H and the other variable is a penicillin ring which is substituted. Variable B is a carbonyl group (the oxygen is not embedded in the chain, but rather a substituent on the chain). Variables Y and Ya are bonds and Z and Za are each hydrogen. Ring A is a benzene ring. Claim 14 is anticipated because Alburn et al. use the prepared compounds to inhibit

Staphylococcus aureus. Claim 27 is anticipated because the final product is prepared by the reaction between the amine portion of pencillanic acid and the carboxylic acid functional group of trypothan (example II is the procedure).

7. Claims 1-4, 8-10, 14, and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Blood et al. Blood et al. teach compound 8-M (columns 41-42). This compound anticipates the elected group because variable R^1 or R^2 is H and the remaining variable of the pair is a substituted hydrocarbon chain. Variable Ya is a $C(O)CH_2$ group, and Za is hydrogen. Variable Y is a bond and Z is hydrogen. Ring A is a benzene ring. Variable B is C(O) (the oxygen is not embedded in the chain, but rather a substituent on the chain). Claim 14 is anticipated because claims 8-9 each cite a pharmaceutical composition comprising compounds of claim 1 (which cover example 8-M). Claim 27 is anticipated because example 5, which uses the procedure of example 3, describes the preparation of example 8-M, only that Ac-Tryptophan Is used instead of Fmoc-tryptophan. The resin is cleaved in example 8, and then compound 8-M is obtained.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Alburn et al. (discussed in 102(b) rejection). The structures in the STN search record render claim 11 obvious because according to *in re Wood* (199 USPQ 137), H vs. methyl on nitrogen is not patentably distinct. H vs. Me is not deemed a patentable advance absent evidence of superior, unexpected results.

Allowable Subject Matter

11. Claim 13 contains allowable subject material.

12. Claims 5-7 and 12-13 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

13. The following is a statement of reasons for the indication of allowable subject matter:Alburn et al. teach the closest prior art. The structures in the STN search report associated with this patent do not anticipate the species of claim 13 because none of them contain a piperazine ring. These compounds do not anticipate claims 5-7 because variable Z is hydrogen, not a cyclic group. Claims 12 are not anticipated because variables R^1 and R^2 are always hydrogen and the penicillin ring.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Noble Jarrell whose telephone number is (571) 272-9077. The examiner can normally be reached on M-F 7:30 A.M - 6:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Noble Jarrell/
Examiner, Art Unit 1624

/James O. Wilson/
Supervisory Patent Examiner
Art Unit 1624